## REMARKS

**Status of the Claims**

Claims 1-45, 47 and 48 were pending and claims 1-14 and 43-45 were under active examination. Claim 1 has been amended as shown above to make explicit that the integral bARE protein comprises is an AB5 LT or CT toxin (*see, e.g.,* page 10, line 15; page 13, 2nd full paragraph) and is soluble (*see, e.g.,* page 11, last paragraph). Accordingly, claim 13 and withdrawn claim 26 have been canceled, without prejudice or disclaimer and claims 14 and 27 have been amended for proper antecedent basis. Claims 3, 11 and withdrawn claim 16 have been amended to remove the recitation "and analogue thereof." Claims 6 and 11 have been amended to clarify that the uncharged agent is a stabilizing agent (*see, e.g.,* page 22, lines 6-7). Claim 12 and withdrawn claim 25 have been amended to clarify the previous recitation of "integrity ratio" (*see, e.g.,* page 12, last paragraph). Finally, withdrawn claims 15, 28 and 37 have been amended to depend from claim 1. As such, the withdrawn method claims contain all the limitations of the composition claims and are subject to rejoinder.

In sum, claims 1-12, 14-25, 27-43, 47 and 48 are pending as shown above and claims 1-12, 14 and 43-45 are under active examination.

**35 U.S.C. § 112, 2nd paragraph**

Claims 1-14 and 43-45 were rejected under 35 U.S.C. § 112, 2nd paragraph as allegedly indefinite. (Office Action, paragraph 3). Claim 1 was alleged to be unclear in what is encompassed by a "substantially integral bARE class protein." *Id.* Claim 3 was alleged to be vague and indefinite for reciting "an analog thereof" and claims 6 and 11 were alleged to be indefinite for reciting an "uncharged agent" and "an analogue thereof." *Id.* Claim 12 was also rejected on the grounds that "integrity ratio" was not clear. *Id.*

Applicants submit that the foregoing amendments obviate the rejections. In particular, claim 1 now makes explicit that the bARE protein is an AB5 CT or LT protein. The term "an analog thereof" has been removed from claim 3 and 6; claim 6 has also been amended to clarify that the uncharged agent is a stabilizing agent and claim 12 has been amended to clarify the "integrity ratio." In view of the foregoing amendments, the rejections may be properly withdrawn.

**35 U.S.C. § 112, 1st paragraph**

Previous claims 1-14 and 43-45 were rejected under 35 U.S.C. § 112, 1st paragraph as not enabled throughout their scope by the as-filed specification. (Office Action, paragraph 5). It was alleged that only compositions comprising an LTK63 protein and arginine phosphate and CHAPS are enabled. *Id.*

To the extent that the foregoing amendments do not obviate the rejection, Applicants traverse the rejection and supporting remarks.

The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. *Ex parte Forman*, 230 USPQ 546 (BPAI 1986). *See, also,* M.P.E.P. § 2164.01, citing *United States v. Telectronics Inc.,* 8 USPQ2d 1217 (Fed. Cir. 1988), *cert. denied,* 490 U.S. 1046 (1989), which held that the disclosure of a single exemplified embodiment and a method to determine other embodiments was enabling, even in the face of evidence that determining additional embodiments might require 6-12 months of effort and cost over $50,000.

The claims as pending are directed to stabilized integral AB5 CT and LT toxin proteins. As well known to the skilled artisan and described in the specification, CT and LT holotoxins were, at the time of filing, known to be similar in structure and function. *See, e.g.,* pages 13-14, noting the well-characterized nature of CT and LT endotoxins and that these two proteins are "structurally, functionally and immunologically" similar, including in that LT and CT are immunologically cross-reactivite. Thus, the skilled artisan would know that any LT or CT protein could be stabilized as described in the specification.

Likewise, the skilled artisan, armed with the teachings of the specification and in view of the state of art, would know that a variety of stabilizing agents other than those exemplified can be used. *See, e.g.,* pages 18-28, including Table 8 showing that various charged and uncharged amino acids were tested and stabilized the claimed bARE proteins. The specification and art teach in detail how to make and use (e.g., by testing) any stabilizing agent and, as such, it is simply a matter of routine experimentation for the skilled artisan to identify suitable stabilizing agents other than those exemplified.

Simply put, it is entirely predictable from the specification (including working examples) that any CT or LT bARE protein could be stabilized using the claimed stabilizing agents and, accordingly, withdrawal of the rejection is in order.

**35 U.S.C. § 102**

Pizza

Claims 1, 2, 6-8, 12-14 and 43-45 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by U.S. Patent Publication No. 2002/0044939 (hereinafter "Pizza"). (Office Action, paragraph 7). It was alleged that Pizza teaches AB5-LTK63 and LTK 72 proteins that are analyzed under non-dissociating conditions which differentiate between integral an dissociated bARE class proteins. *Id.*

The pending claims are directed to integral AB5 LT or CT holotoxins. By contrast, Pizza relates to stability of an A subunit of LT in isolation. Thus, Pizza does not describe or demonstrate the specifically claimed composition and the rejection cannot be sustained.

Pronk

Claims 1, 2, 6-8, 12-14 and 43-45 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Pronk et al. (1985) *J. Biol.. Chem.* 260(25):13580-13584 (hereinafter "Pronk"). (Office Action, paragraph 8). It was alleged that Pronk teaches substantially integral crystals of bARE proteins. *Id.*

Whereas the pending claims are drawn to soluble holotoxins, Pronk is admittedly drawn to crystalline LT. Accordingly, Pronk does not describe or demonstrate the claimed subject matter and withdrawal of the rejection is in order.

## CONCLUSION

In view of the foregoing, Applicants submit that the claims are in condition for allowance.

Please direct all further communications regarding this application to:

Helen Lee
NOVARTIS VACCINES AND DIAGNOSTICS, INC.
Intellectual Property – X100B
P. O. Box 8097
Emeryville, CA 94662-8097
Customer No: 27476

Respectfully submitted,

Date: September 28, 2009

By: 

Dahna S. Pasternak
Registration No. 41,411
Attorney for Applicant

NOVARTIS VACCINES AND DIAGNOSTICS, INC.
Intellectual Property – X100B
P. O. Box 8097
Emeryville, CA 94662-8097
Tel.: (650) 493-3400; Fax: (650) 493-3440